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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08 398,555	03 03 1995	LINDA G. CIMA	MIT6210	7254

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EXAMINER

RUSSEL, JEFFREY E

ART UNIT

PAPER NUMBER

1654

DATE MAILED: 03 31 2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

08/398,555

Applicant(s)

CIMA ET AL

Examiner

Jeffrey E. Russel

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 February 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 14-17 and 32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14-17 and 32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☒ The proposed drawing correction filed on 21 July 1997 is: a) ☒ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other

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1. The request filed on February 27, 2003 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/398,555 is acceptable and a CPA has been established. An action on the CPA follows.

The amendment after final rejection filed January 2, 2003 has been entered.

2. Claims 14-17 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 14 and 32 are unclear as to whether they require a positive process step of attaching the tether to the substrate using the specific attachment agents, or if the claims instead recite a product-by-process definition of the attachment between the tether and the substrate. Claims 14 and 32 are indefinite because they require covalent attachment of the tether to the substrate; however, one of the specified attachment means, avidin-biotin, does not constitute covalent attachment. Claims 14 and 32 are indefinite because their Markush terminology is incorrect. In each claim, "and maleimide, carbodiimide" should be changed to "maleimide, and carbodiimide".

3. Claim 32 is objected to because of the following informalities: At claim 32, page 18 of the amendment filed January 2, 2003, line 7, "compositio" should be changed to "composition".

Appropriate correction is required.

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993), *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985), *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982), *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970), and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 14-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,906,828 and further in view of Applicants' admission of the prior art at page 12, lines 1-12, of the specification. Although the conflicting claims are not identical, they are not patentably distinct from each other. It is the examiner's position that a one-way test is appropriate for obviousness-type double patenting. The claims of the '828 patent do not recite an attachment agent which is cyanogen bromide, succinimide, aldehyde, tosyl chloride, avidin-biotin, epoxide, or maleimide. Applicants admit at page 12, lines 1-12, of the specification that cyanogen bromide, succinimide, aldehydes, tosyl chloride, avidin-biotin, epoxide, and maleimides are standard immobilization chemistries which are well known in the art. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to attach the tethers recited in the claimed invention of the '828 patent to the substrate using standard immobilization chemistries which are well known in the art, including cyanogen bromide, succinimide, aldehydes, tosyl chloride, avidin-biotin, epoxide, and maleimides, because the claims of the '828 patent require covalent attachment yet are not limited to any particular attachment agents and because it is routine to use standard immobilization chemistries which are well known in the art to achieve only the expected immobilization because of their familiarity and predictability to the artisan.

6. Claim 32 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 20 of U.S. Patent No. 6,045,818 and further in view

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of Applicants' admission of the prior art at page 12, lines 1-12, of the specification. Although the conflicting claims are not identical, they are not patentably distinct from each other. It is the examiner's position that a one-way test is appropriate for obviousness-type double patenting.

The claim of the '818 patent does not recite an attachment agent which is cyanogen bromide, succinimide, aldehyde, tosyl chloride, avidin-biotin, epoxide, or maleimide. Applicants admit at page 12, lines 1-12, of the specification that cyanogen bromide, succinimide, aldehydes, tosyl chloride, avidin-biotin, epoxide, and maleimides are standard immobilization chemistries which are well known in the art. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to attach the tethers recited in the claimed invention of the '818 patent to the substrate using standard immobilization chemistries which are well known in the art, including cyanogen bromide, succinimide, aldehydes, tosyl chloride, avidin-biotin, epoxide, and maleimides, because the claims of the '818 patent require covalent attachment yet are not limited to any particular attachment agents and because it is routine to use standard immobilization chemistries which are well known in the art to achieve only the expected immobilization because of their familiarity and predictability to the artisan.

7. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

8. Claims 14-17 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application '616. The WO Patent Application '616 teaches a support surface, e.g., a biocompatible polymer such as polyurethane, polyester, skin, or cellulose in any desired shape including shapes suitable for implantation (page 7, line 28 - page 9, line 16) to which is covalently attached biomolecules such as ECGF, FGF, PDGF, and collagen (page 7, lines 14-27)

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through a spacer preferably made from a polyethylene oxide at least 25 angstroms long, e.g. having a size of 1450 daltons which is equivalent to a backbone length of about 99 atoms (page 7, lines 2-8, and pages 20-24), i.e. a tether. The spacers can be attached to the support surface using thermochemical reactive groups, including alkylaldehyde, maleimides and N-oxy succinimide carboxylic esters (see, e.g., page 11, lines 14-22, and claims 4 and 21). Animal cells such as endothelial cells are cultured on the carriers (pages 20-24). The invention permits the loading density of biomolecules to a support surface to be increased (page 14, lines 27-30). Because the biomolecules are covalently attached to the support surface of the WO Patent Application '616, inherently they will not be able to be internalized by the cells. Because the structure and chemical composition of carriers of the WO Patent Application '616 are the same as is recited in Applicants' claims, and because of the higher biomolecule loading density achieved by the WO Patent Application '616, inherently the rate of target cell growth will be enhanced in the WO Patent Application '616 to the same extent claimed by Applicants.

9. Claims 14-17 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application '616 as applied against claims 14-17 above, and further in view of Applicants' admission of the prior art at page 12, lines 1-12, of the specification. The WO Patent Application '616 does not teach all of the attachment agents recited in claims 14 and 32. Applicants admit at page 12, lines 1-12, of the specification that cyanogen bromide, succinimide, aldehydes, tosyl chloride, avidin-biotin, epoxide, and maleimides are standard immobilization chemistries which are well known in the art. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to attach the spacers of the WO Patent Application '616 to the support surfaces using standard immobilization chemistries which are

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well known in the art, including cyanogen bromide, succinimide, aldehydes, tosyl chloride, avidin-biotin, epoxide, and maleimides, because the WO Patent Application '616 is not limited to any particular attachment agent (see, e.g., page 5, lines 1-5, and page 10, lines 1-12) and because it is routine to use standard immobilization chemistries which are well known in the art to achieve only the expected immobilization because of their familiarity and predictability to the artisan.

10. Applicant's arguments filed January 2, 2003 have been fully considered but they are not persuasive.

Obviousness-type double patenting rejections over U.S. Patent Nos. 5,906,828 and 6,045,818 are maintained over the amended claims. The examiner agrees that the nature of the attachment agent can play an important function in directing the orientation and spacing of the tether and the attached growth effector molecule, and can be important for obtaining a substantially optimum activity of the growth effector molecule. However, as the rejected claims do not require any particular orientation or spacing for the tether and attached growth effector molecule, and do not require that substantially optimum activity of the growth effector molecule be achieved, this argument does not distinguish over the prior art. Patentability must be based upon claimed, not unclaimed, differences over the prior art. Further, Applicants are claiming the use of standard immobilization chemistries which are well known in the art (see Applicants' admission of the prior art at page 12, lines 1-12, of the specification). Applicants have not shown that the standard immobilization chemistries which are well known in the art can not be used to achieve particular orientation or spacing for the tether and attached growth effector

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molecule and can not be used to achieve substantially optimum activity of the growth effector molecule.

The obviousness rejections based upon Herweck et al in view of Merrill (U.S. Patent No. 5,171,264) and upon Herweck et al in view of Merrill (U.S. Patent No. 5,171,264) and further in view of Mikos set forth in the Office action mailed October 29, 2002 are withdrawn in view of the new claim limitations requiring attachment of the tether to the substrate using cyanogen bromide, succinimide, aldehyde, tosyl chloride, avidin-biotin, epoxide, maleimide, or carbodiimide. Merrill teaches only the use of ionizing radiation to attach its PEO star molecules to its support surface, and teaches away from the use of other known crosslinking techniques (see, e.g., column 3, lines 11-14 and 47-55). Accordingly, there is no motivation to substitute Applicants' claimed attachment agents for the attachment means of Merrell.

The anticipation rejection based upon the WO Patent Application '616 is maintained. The WO Patent Application '616 teaches examples of succinimide, aldehyde, and maleimide attachment agents claimed by Applicants (see page 11, lines 21-22, 17, and 21, respectively, of the WO Patent Application '616). The WO Patent Application '616 is not limited to hydrophobic photochemical groups, and hydrophobic photochemical groups do not constitute the reference's only disclosed "proper" linking groups - see, e.g., page 11, lines 14-22, and claims 4 and 21. Further, the disclosure of a reference is not limited to the reference's most preferred embodiments. See MPEP 2123. The WO Patent Application '616's use of qualifying terms such as "generally" (see, e.g., page 10, line 2), "for the most part" (see, e.g., page 11, line 10), and "desirably" (see, e.g., page 10, line 9) shows that the WO Patent Application '616 is not limited to the use of photoreactive and/or hydrophobic groups to attach its spacers to its support

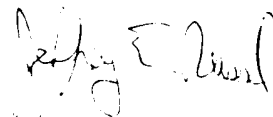


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surface. Accordingly, use of standard immobilization chemistries to form the biocompatible coatings of the WO Patent Application '616 as set forth in the above obviousness rejection is deemed to be prima facie obvious. As to whether or not the WO Patent Application '616 "implicitly defines the reactive group linking the spacer to the biomolecule to be a hydrophilic group", this does not affect the rejection because the rejected claims contain no limitations which would require the reactive group linking the spacer to the biomolecule to be other than a hydrophilic group. Patentability must be based upon claimed, not unclaimed, differences over the prior art.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel  
Primary Patent Examiner  
Art Unit 1654

JRussel  
March 28, 2003